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Evolution of a CDC Public Health Research Agenda for Low-Risk Prostate Cancer

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Abstract

Men with prostate cancer face difficult choices when selecting a therapy for localized prostate cancer. Comparative data from controlled studies are lacking and clinical opinions diverge about the benefits and harms of treatment options. Consequently, there is limited guidance for patients regarding the impact of treatment decisions on quality of life. There are opportunities for public health to intervene at several decision-making points. Information on typical quality of life outcomes associated with specific prostate cancer treatments could help patients select treatment options. From 2003 to present, the Division of Cancer Prevention and Control at CDC has supported projects to explore patient information-seeking behavior post-diagnosis, caregiver and provider involvement in treatment decision making, and patient quality of life following prostate cancer treatment. CDC's work also includes research that explores barriers and facilitators to the presentation of active surveillance as a viable treatment option and promotes equal access to information for men and their caregivers. This article provides an overview of the literature and considerations that initiated establishing a prospective public health research agenda around treatment decision making. Insights gathered from CDC-supported studies are poised to enhance understanding of the process of shared decision making and the influence of patient, caregiver, and provider preferences on the selection of treatment choices. These findings provide guidance about attributes that maximize patient experiences in survivorship, including optimal quality of life and patient and caregiver satisfaction with information, treatment decisions, and subsequent care.

Introduction

More than 200,000 men are diagnosed with prostate cancer annually,[1] the majority diagnosed with localized disease.[2,3] Treatment choices available to newly diagnosed, early-stage prostate cancer patients include radical prostatectomy; brachy-therapy; external beam radiation; and active surveillance (AS).[3] Most of these treatments can affect health-related quality of life (QOL)[3] as a result of significant morbidity and physical side effects. However, AS may be associated with increased anxiety, missed opportunity for cure, risk of

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progression or metastasis, more complex subsequent treatment, frequent medical exams, and periodic biopsies that may result in complications.[4]

Given the number of choices available for active treatment and their potential side effects, new patients may experience difficulty deciding what treatment is best suited for their cancer, personal preferences and health status, and home support environment, and information on typical QOL outcomes associated with prostate cancer treatments could guide patients in selecting treatment options. For many men, treatment discussions and decisions may take place at home with family.[5] Treatment choices are inevitably influenced by three decision makers: the patient; the physician; and (when present) the patient's family (e.g., spouse/partner or caregiver).[6] In 2003, there were no known published prospective studies that examined the influence of this triad of decision makers on treatment decisions or prospectively explored how knowledge, preferences, and interactions among prostate cancer patients, caregivers, and treating physicians ultimately influence treatment choice, QOL, and treatment satisfaction.

In 2003, CDC supported two Prevention Research Centers (University of Washington and Emory University) to prospectively examine men's selection of prostate treatment, caregiver involvement, and patient, caregiver, and physician perceptions of patient QOL. These studies focused on information-seeking behavior, how treatment decisions are made, and patient-reported QOL 12 months following diagnosis. Manuscripts from these studies, published in 2006–2013, document the importance of patient characteristics in evaluating patient QOL[7] and treatment decision making,[8,9] factors that influence treatment decisions,[10] and the impact of race and residence on these decisions.[9] Other studies elucidated patient experiences with second opinions,[11] QOL at 12 months of follow-up,[12] use of complementary and alternative medicine,[13] and racial differences in treatment-based beliefs and coping.[14] Additional studies explored physician–caregiver interactions[15] and caregiver roles[16] in the decision process, as well as caregiver burden.[17–19] Studies also examined the process of building a collaborative study team[20] and the agreement of data ascertained from multiple sources.[21]

The predominant finding was that men diagnosed with low-grade tumors, who would likely die from other causes before disease progression, almost always opted for active treatment regimens. Many of the men who chose curative treatment were likely candidates for an AS protocol where low-risk prostate cancer is closely monitored but not treated immediately. AS allows men to avoid the potential side effects of radiation and surgery (e.g., urinary incontinence, impotence), reduces risk of treatment of small indolent cancers, and has minimal effect on QOL.[22] Patients may opt for active treatment at any time, or physicians can intervene if the tumor profile worsens. Data showed that 79% of men considering AS reported a physician recommendation.[9] These findings highlighted the need for further examination of factors associated with recommending, accepting, and participating in an AS protocol. This article reviews CDC-supported work in prostate cancer and describes the evolution of its research agenda.

Focus on Active Surveillance

State of the Science Conference

In 2009, building on findings from QOL research, CDC initiated discussions with the Office of Medical Applications Research, NIH, and the National Cancer Institute to discuss interest in convening a State of the Science (SOS) conference to assess the availability of published evidence to distinguish patients who may be good candidates for AS. Subsequently, the Office of Medical Applications Research entered into partnership with CDC, the National Cancer Institute, and the American Cancer Society to outline an agenda for the conference. Through review of the literature,[23] clinical profiles, and tumor and behavioral characteristics presented by leaders in the field, the conference panel was charged with synthesizing the state of current knowledge, identifying gaps in knowledge, and articulating a research agenda.

The NIH SOS Conference: Role of Active Surveillance in the Management of Men with Localized Prostate Cancer was held December 2011. A monograph of conference proceedings[24] summarized all evidence presented at the conference along with a reprint of the panel consensus statement. The panel concluded that there was not sufficient evidence to allow definitive determination of the optimal characteristics of prime AS candidates, but that research needs be conducted to allow physicians and researchers to identify men appropriately.[25] Such an AS research agenda needs to

1. determine which men are the most appropriate candidates;
2. determine what is the optimal protocol for surveillance;
3. determine how to best communicate AS as an option to patients;
4. develop methods to assist patient decision making;
5. clarify patient reasons for accepting or rejecting AS as a treatment strategy; and
6. conduct multicenter studies that incorporate community settings and partners.

The SOS conference concluded that AS be offered more frequently to more patients with low-risk prostate cancer.[25] These recommendations can be used to generate discussion among physicians about greater use of AS among patients with low-risk tumor profiles, foster research that assists in better characterizing optimal candidates for AS, and assist in the development of decision aids that present AS with similar weight and detail as active treatments.

Assessment of Patient Perceptions of Active Surveillance

Testimony presented during the SOS conference highlighted qualitative research that compared AS, surgery, and radiation therapy.[26] Results showed that information about treatment options can be presented such that men accepted AS as an option in relation to the major treatments[26]; however, no literature specifically asked patients and caregivers what types of information their physicians needed to provide to make AS an equally viable option to active treatment.

In 2009, concomitant with SOS planning talks, CDC funded two Prevention Research Centers (University of Texas Health Science Center at Houston and Emory University) to determine, from the patient and caregiver perspective, desired talking points and preferred content about AS. These studies could provide the basis for developing an educational intervention for physician discussion with patients about AS and the preferred patient content to include in conversations that would aid in making AS an acceptable alternative.

Study 1: Acceptability of Active Surveillance as a Treatment Choice for Prostate Cancer Among U.S. Men

The University of Texas Health Science Center at Houston assembled convenience samples of African American, Hispanic, and non-Hispanic white men recruited from Houston and El Paso, aged 40–70 years, who had a prostate-specific antigen test within the previous 2 years, and no history of prostate cancer.[27] Men and identified caregivers participated in a series of focus groups segmented by gender; race/ethnicity; and language (English, Spanish), conducted between May 2010 and February 2011. Groups discussed how participants would make treatment decisions if they (or their partners) were diagnosed with early-stage localized prostate cancer, what information would be needed to make an informed decision, how they would evaluate information, and who they would involve in the decision-making process.[27] Additionally, following a separate recruitment of newly diagnosed patients, 15 men who selected AS and 15 men treated with surgery or radiation participated in telephone interviews about discussed and considered treatment options, patient descriptions of AS, how the decision was made, physician recommendations, and their partner's role in decision making.[28]

Study 2: Active Surveillance Attitudes and Perceptions: Decision Making by Men and Their Significant Others for Early-Stage Prostate Cancer

Emory University's AS Attitudes and Perceptions study, conducted from September 2009 through September 2012, utilized a multicenter, mixed-methods design, combining both qualitative and quantitative methodologies to assess factors men and their caregivers regard as vital to informed decision making about prostate cancer therapies. Separate patient (n=214) and caregiver (n=188) focus groups were held across six locations.[29]

Results from the above studies suggested that information about the nature of prostate cancer, available options, the benefits and harms of the options, and their likelihood of occurrence should be included in decision aids to assist patients in their discussions with providers and expressing their outcome preferences. Decision aids should also offer prompts for questions to doctors and messages designed to reinforce the importance of sharing one's preferences.[27] Men who made treatment decisions displayed receptiveness to AS when fully informed about this option,[28] and described it as an organized process with a rigorous and reassuring protocol of periodic testing, with potential for subsequent and timely decision making about any future treatment, and as an option for prolonging good health and function. Rationales for choosing AS included “buying time” without experiencing adverse effects of treatment, waiting for better treatments, trusting their physician's monitoring, and perceiving their cancer as very low risk.[28] The AS Attitudes and Perceptions study revealed that men were more concerned about treatment side effects whereas caregivers were more

interested in a treatment's potential to increase survival and preferred that primary care providers (versus urologists or radiologists) should discuss all prostate cancer options with patients (particularly AS), as primary care providers were perceived as neutral advocates for patients.[30]

Lessons Learned

CDC-supported work revealed that the majority of men newly diagnosed with prostate cancer opt for surgery or radiation. The SOS conference panel recommended that AS be offered to more men. Information was needed to help patients and caregivers in their consideration of AS. The conference garnered insights into how to initiate discussions with patients about AS and elicited patient and caregiver concerns regarding AS and other treatment choices. Patients taught that being well informed about AS facilitates acceptability and that some men prefer to have such discussions with primary care physicians.

Putting It Together

Future CDC research may include investigations about the various components of the AS conversations, methods to support patient treatment decision making, and ensuring that all patients are informed and educated about all of their treatment options. Additional studies may explore barriers and facilitators of AS as a viable treatment option and ensure that it is presented to appropriate patients with the same emphasis as active treatments. Consistent with the SOS agenda to develop methods to assist patient decision making, CDC sought to explore the design of a treatment decision aid with a substantial AS component that would acknowledge sociodemographic and cultural differences, attend to patient informational needs and consider patient desired goals and outcomes, facilitate collaborative involvement of both the patient and caregiver in the decision process, and address the role of the provider. AS is frequently given little attention in decision aids, and an effective decision aid could provide more-complete and accurate descriptions of this option and represent it as an appropriate strategy for men with low-risk localized prostate cancer who are concerned about aggressive treatment complications.[31] Decision aids should also meet quality standards for content, development processes, and effectiveness—demonstrating their ability to increase knowledge about treatment options and improve harmony between patient values and the selected treatment.[32]

Study 1: Development and Evaluation of an Interactive Clinical Decision Dashboard to Support Treatment Decisions for Men With Low-Grade, Local-Stage Prostate Cancer

In 2014, CDC funded the University of Rochester to develop and test an interactive multimedia decision aid in the form of a clinical decision dashboard,[33] designed to improve the quality of clinical decision making for initial treatment of patients with newly diagnosed, low-risk prostate cancer. The tool will be designed to allow for multiple considerations (tumor characteristic, patient preferences, caregiver input) during decision-making deliberations with the goals of

1. informing recently diagnosed men of their treatment options, including AS, and helping them to determine their treatment preferences; and

2. supporting providers by providing up-to-date information summaries about treatment outcomes tailored for individual patient demographics and tumor characteristics.

A clinical trial will be conducted to compare the effects of the prostate decision dashboard versus usual care on patient knowledge regarding the management and treatment options available, measures of the decision-making process including decisional conflict and shared decision-making process, the selected treatments, and 6- and 12-month outcome assessments of clinical status, decisional regret, and cancer-related QOL.

Impact of CDC Research Agenda

Since 2003, CDC has engaged in a prostate cancer public health research agenda that has informed understanding of the needs and experiences of survivors of localized prostate cancer. This research has identified the following priorities for public health:

1. engaging in education to effectively inform patients and caregivers about the various available treatments and support the decision-making process, particularly among men who are traditionally medically underserved;
2. providing decision tools for patients, caregivers, and providers to promote effective conversation about all treatment options, including AS;
3. engaging in regular surveillance and evaluation of AS uptake, including sociodemographic, QOL, and clinical measures;
4. reducing loss to follow-up of men on AS protocols; and
5. tracking and evaluating decisions to terminate an AS protocol, including clinical status and QOL outcomes pre– and post–active treatment.

In the 4 years since the SOS conference, use of AS for patient management has grown in popularity,[34,35] and research has proliferated in a number of areas, including better characterization of suitable AS candidates,[36,37] defining appropriate standardized AS protocols,[38] risks associated with monitoring,[39] and criteria for disease progression.[40] Recent studies have reviewed the quality of care received by patients undergoing AS,[41] and new tools to safely monitor low-risk prostate cancer[42,43] are being proposed, such as use of biomarkers to better stratify risk of disease progression.[44–46] New studies are beginning to quantify the number of men who are lost to follow-up while on AS protocols.[47] Overall knowledge of who needs to be offered AS and how to monitor them has improved.

Future research may more explicitly characterize an appropriate AS protocol for African American men. Recent literature suggests that the tumors of African American men on AS initially characterized as low risk are often upgraded on serial biopsy,[48] have worse pathologic characteristics,[49] and that disease is more likely to recur following surgery[50] compared with men of other races, although these results have not been confirmed in other studies.[51] These findings have raised the question of whether AS is appropriate for African American men, if this group requires more-stringent surveillance strategies, or whether more extensive initial clinical indicators to determine eligibility for AS are warranted. Methods to

effectively determine the potential aggressiveness of small tumors and the exact protocols for monitoring all men are needed.

CDC's early prostate cancer work highlighted that poor physician communication was associated with men not making a treatment choice, especially among African American men.[9] Education about active treatments, AS, potential for complications and recurrence, physical side effects, and impact on QOL is still needed by all decision makers to inform choices made by men and their caregivers.[52] CDC-funded work has served as a model for assessing the perspectives of patient, caregiver, and physician, promoting discussion of AS, and developing tools to assist patient–physician conversations. Improving the quality of survivorship among men diagnosed with localized prostate cancer will include identifying the correct patients for certain treatments, improving patient knowledge and awareness about treatment choices, and understanding the impact and roles of providers and caregivers in treatment decision making. CDC and its partners remain committed to exploring aspects of prostate cancer treatment decision making that present opportunities to improve cancer survivorship, reduce overtreatment, and enhance QOL of patients and caregivers.

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